

Applicants: Peter S. Linsley et al.  
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*Calif sub*  
receptor on the CD28 positive T cells with B7 antigen  
and thereby inhibiting T cell proliferation.

- Calif sub*
- 7. (amended) The method of claim 6, wherein said moiety is an immunoglobulin constant region.
- Calif sub*
- 8. (amended) The method of claim [6] 3, wherein said derivative comprises a fusion polypeptide having a first amino acid sequence containing amino acid residues from about position 1 to about position 215 of the amino acid sequence corresponding to the extracellular domain of B7 antigen and a second amino acid sequence corresponding to the hinge, CH2 and CH3 regions of human immunoglobulin Cγ1.
- 9. (amended) The method of claim 1, wherein said B7 antigen is immobilized to crosslink CD28 receptor on said T cells.
- 10. (amended) The method of claim 9, wherein said T cells are reacted with CHO cells expressing B7 antigen.
- 16. (amended) The method of claim 15, wherein said anti-CD antibody is anti-CD2 or anti-CD3 monoclonal antibody.
- Calif sub*
- 17. (amended) The method of claim 1, wherein said T cells are reacted with B cells expressing B7 antigen [and said T cell responses are stimulated].
- 18. (x2 amended) The method of claim 1, wherein the CD28 positive T cells are reacted with the B7 antigen in soluble form [and the T cell responses are inhibited].

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CO2  
CO1  
sub  
H57  
--19. (X3 Amended) A method of [regulating functional] inhibiting CD28 positive T cell [responses of] proliferation [T cells] comprising reacting B7 positive cells with a monoclonal antibody designated BB-1 or a F(ab)<sub>2</sub> fragment thereof or the CD28Ig fusion protein so as to bind the monoclonal antibody or the F(ab)<sub>2</sub> fragment thereof or the CD28Ig fusion protein with B7 positive cells and thereby blocking B7-T cell interaction and inhibiting CD28 positive T cell proliferation.

CO4  
--23. (amended) The method of claim 21, wherein said monoclonal antibody is reactive with a fusion protein comprising a polypeptide having a first amino acid sequence containing amino acid residues from about position 1 to about position 215 of the amino acid sequence corresponding to the extracellular domain of B7 antigen and a second amino acid sequence corresponding to the hinge, CH2 and CH3 regions of human immunoglobulin Cγ1.

--24. (amended) The method of claim 23, wherein said fusion protein is B7Ig corresponding to the amino acid sequence encoded by DNA having ATCC No. 68627.

--28. (amended) The method of claim [27] 26, wherein said fragment or derivative contains at least a portion of the extracellular domain of the CD28 receptor.

CO5  
--29. (amended) The method of claim [27] 26, wherein said fragment is a polypeptide having an amino acid sequence containing amino acid residues from about position 1 to

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about position 134 of the amino acid sequence corresponding to the extracellular domain of CD28 receptor.

COB  
CONF  
--30. (amended) The method of claim [27] 26, wherein said derivative comprises a fusion polypeptide having a first amino acid sequence corresponding to the extracellular domain of CD28 receptor and a second amino acid sequence corresponding to a moiety that alters the solubility, affinity and/or valency of said CD28 receptor for binding to B7 antigen.

--31. (amended) The method of claim 30, wherein said moiety is an immunoglobulin constant region.

--32. (amended) The method of claim [27] 26, wherein said derivative is a CD28 fusion protein comprising a polypeptide having a first amino acid sequence containing amino acid residues from about position 1 to about position 134 of the amino acid sequence corresponding to the extracellular domain of CD28 receptor and a second amino acid sequence corresponding to the hinge, CH2 and CH3 regions of human immunoglobulin C $\gamma$ 1.

COB  
--35. (x2 amended) A method for preventing the binding of the CD28 receptor to the B7 antigen [so as to inhibit functional T cell responses] comprising contacting CD28 positive T cells with an anti-CD28 monoclonal antibody which recognizes and binds a determinant site to which the monoclonal antibody 9.3 is directed so as to prevent binding of the receptor to the B7 antigen.

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67  
--37. (amended) The method of claim [36] 35, wherein [said ligand] the anti-CD28 monoclonal antibody is a Fab fragment of anti-CD28 monoclonal antibody.

--38. (amended) The method of claim [36] 35, wherein said antibody is 9.3 monoclonal antibody produced by hybridoma ATCC No. HB10271.

--39. (amended) The method of claim [36] 35, wherein said anti-CD28 antibody is reactive with a fusion protein comprising a polypeptide having a first amino acid sequence containing amino acid residues from about position 1 to about position 134 of the amino acid sequence corresponding to the extracellular domain of CD28 receptor and a second amino acid sequence corresponding to the hinge, CH2 and CH3 regions of human immunoglobulin Cyl.

se  
F3  
--40. (amended) The method of claim 39, wherein said fusion protein is CD28Ig fusion protein corresponding to the amino acid sequence encoded by DNA having ATCC No. 68628.

sub  
H7  
--41. (Amended) [The method of claim 35,] A method for preventing the binding of the CD28 receptor to the B7 antigen comprising contacting CD28 positive T cells with a fragment or derivative of the extracellular domain of the B7 antigen so as to bind the CD28 receptor on the CD28 positive T cells with the fragment or derivative of the extracellular domain of the B7 antigen thereby preventing binding of the receptor to the B7 antigen.

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cont  
cont*  
--42. (x2 amended) The method of claim 41, wherein said derivative is a B7Ig fusion protein comprising an amino acid sequence containing amino acid residues from about position 1 to about position 215 of the amino acid sequence corresponding to the extracellular domain of B7 antigen.

*2* Please add new claim 78 as follows.

*68-74*  
--78. (new) A method of inhibiting CD28 positive T cell activation comprising reacting B7 positive cells with a CD28 antigen so as to bind the B7 positive cells with the CD28 antigen thereby inhibiting T cell activation.

REMARKS

Applicants respectfully request entry of the Amendment under 37 C.F.R. §1.116 in response to July 12, 1993 Office Action and Petition for a two month extension of time dated December 13, 1993.

Claims 1, 3, 5-10, 15, 17-24, 26-32, 35-42, 47, 49, 51-57, 63-65, 67-77 were pending. Claims 67-76 have been withdrawn as directed to a non-elected invention. Claims 20-22, 26-27, 36, 47, 49, 51-57, 63-65 and 77 have been canceled without prejudice. Claims 1, 7, 8, 9, 10, 16, 17, 18, 19, 23, 24, 28, 29, 30, 31, 32, 35, 37, 38, 39, 40, 41, and 42 have been amended. New claim 78 has been added. Accordingly, claims 1, 3, 5-10, 15, 17-19, 23-24, 28-32, 35, 37-42, and 78 are presently being examined.

Support for the changes to claims 1, 7, 8, 9, 10, 16, 17, 18, 19, 23, 24, 28, 29, 30, 31, 32, 35, 37, 38, 39, 40, 41, and 42 may be